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REMARKS ON ACUTE MYELITIS, AND REPORT OF A CASE OF TUBERCULOUS MENINGO-MYELITIS.

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The question whether acute myelitis is a rare disease or not may be answered in the affirmative or the negative, depending entirely upon what is included under such a designation. If we include acute transverse myelitis, acute diffuse myelitis ascending and descending, acute disseminated myelitis, acute anterior poliomyelitis, as Leyden and Goldscheider do, it is the commonest disease of the central nervous system, for it takes in diseases which are well recognized as either pathological or clinical entities, such as infantile paralysis, Landry's paralysis and acute hemorrhagic softening associated with disease of the blood and the vessels. It includes also the destructive lesions accompanying trauma, diminution of atmospheric pressure (caisson disease), and disease of the abdominal aorta leading to occlusion, and obliteration of the vessels leading to softening. From the clinical standpoint these cases are truly myelitis. But if we make circulatory manifestations of inflammation the criterion by which to judge whether or not there is any inflammation, many of these conditions must be excluded. For instance, softening resulting from trauma, obliteration of the vessels, diseases of the blood such as anemia, edema, inflammatory or otherwise. From a pathological standpoint, however, such conditions are to be differentiated by the absence of changes in the circulation typical of inflammation. If they are differentiated, and not included under the caption of acute myelitis, then the disease is extremely rare. If they are included—and they are usually clinically, for they can not be distinguished by the clinical picture alone, then the disease is, as has just been said, not uncommon. Whether or not it is a common disease differs also with our conception of acute myelitis from an etiological standpoint.

If we consider acute myelitis to be an inflammatory state of the spinal cord due to infection or intoxication, the morbid process being caused either directly by the action of the microbes and their toxins acting upon the medullary parenchyma, or indirectly through the circulatory system, then the disease is really very rare. As a matter of fact, primary acute myelitis (leaving out of consideration anterior poliomyelitis), whether it be transverse, diffuse or disseminated, is a rare disease and nearly always due to infections or intoxications.

The infectious organisms that produce such myelitis are numerous. Those that have been found in the inflammatory focus are the streptococcus, the staphylococcus (at least two varieties) the pneumococcus, and a special diplococcus described by Buzzard and Russell. In the case described herewith, one of acute meningo-myelitis, the tubercle bacillus was found in the inflammatory focus.

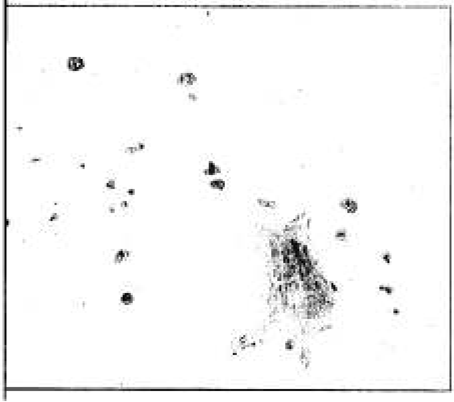
Mere enumeration of the acute diseases that have been closely followed by myelitis, and with which it is safe to assume the myelitis stands in causal relationship, shows that the number of organisms capable of causing myelitis is not exhausted by those above mentioned. Thus it has been shown that myelitis follows tonsilitis, dysentery, erysipelas, typhoid fever, gonorrhea, cystitis, puerperal fever, pneumonia, influenza, rabies, tetanus, phlegmonous paronychia; to mention no others. Undoubtedly, in many instances the germ itself does not produce the disease, but the toxins which they manufacture cause it. It is not safe however, to assume that the germ does not cause the disease *per se,* and by its local action, because it is not found in the focus after death, for it is well known that the germ begins to disintegrate and disappear the moment it has exercised its malign effect. The fact that the germ is sometimes found on microscopical examination, as it was in the case reported herewith, shows that at least some of the cases of acute inflammation of the cord are dependent upon the immediate presence of the organism itself.

The patient whose history I present was admitted to the City Hospital April 19, 1898. She was a Polish Jewess, twenty years old. So far as could be learned, her family history was negative. Her personal history was likewise uninteresting: a hard-working, underfed corset-maker, who denied the use of spirits and in whom there were no evidences of venereal infection. When a child she had measles, but since then she had been entirely free from illness. Her first child was born in the hospital two months after the onset of the illness which caused the patient's death. This illness began about three months before its fatal termination. She said that the first manifestation of the disease was that one morning on arising the right hand "was sore;" which being interpreted means that the second metacarpo-phalangeal articulation was red and swollen, and that the finger could not be moved because of the swelling and of the pain which attempts at movement caused. Even when the extremity was at rest, this joint was the seat of sharp, stinging pain. This pain continued for two or three days; then the right elbow became painful and somewhat swollen. The pain and swelling subsided slowly, and after a day or two the right shoulder became affected in a similar way. In two or three days the swelling and pain of the shoulder began to subside, and then she complained of pain in the middle of the back. The pain and stiffness of the back were not so unbearable as the pain in the other joints. Moreover, they disappeared in a few days. The anterior surface of the right thigh and the right groin then got painful. Later, the right knee became stiff and swollen, and she soon was unable to walk or take care of herself. She was then taken to Bellevue Hospital and remained there for three weeks under treatment for rheumatism, she said. The record of her case while in that institution has not been seen, but when she was transferred to the City Hospital from Bellevue it was noted there was a bedsore over the sacrum, one over each iliac crest, one over the anterior superior spinous process, one over the left trochanter, and one over the right knee. All these sores were extremely painful, especially that on the back. From all of them pus discharged freely. She remained in the ward to which she was at first admitted for a short time only, for it soon became apparent that she was about to give birth. She was transferred to the Maternity Hospital, and was delivered of a child that is now alive. She had no labor pains, but during the birth she complained of great pain in the joints, due apparently to inability to separate the legs and to remain on the back. A few days after her confinement she was sent to one of my wards, where the following notes were made:

"The patient who is extremely emaciated, lies on the back, the feet and toes semi-flexed, and the knees and thighs firmly flexed. When attempt is made to overcome the flexion the patient complains bitterly. The legs and thighs are very much wasted. [This was not considered other than part of the general emaciation, although it is very probable that it was likewise due to disease of the ventral horns which was afterwards found.] The knee-jerks can not be elicited, nor can the spasticity of the legs be overcome. The absolute fixation of the lower extremities is thought to be due in great measure to involuntary efforts at restraint to avoid the pain that movement causes. The patient is wholly unable to move any part of the lower extremities, but she complains of painful twitchings of the muscles and of uncontrollable drawing up of the legs. She is incontinent of urine, most of the time, but the rectal sphincter seems to functionate normally. There are no elicitable disturbances of sensibility. [It was difficult to be certain of this on account of her fear that she was going to be hurt by the examination.] The sore on the back, over the sacrum, is as large as two hands and it has destroyed the soft tissues down to the bone. The finger or probe can be admitted for a distance of from three to four inches. This procedure is very painful, causing liberal discharge of pus, just as if a new well had been opened up. The other bedsores enumerated above are of the extremest kind. The upper extremities are emaciated and slightly rigid, but not devoid of voluntary power. There is no deformity of the spine. The cranial nerves are unaffected, and the patient gives a lucid account of her illness." Careful examination of the thoracic and abdominal viscera failed to reveal anything pathological. When first admitted to the hospital, the records show that she was without fever. About two weeks before death she began to have rigors and irregular elevation of temperature, and to show the customary phenomena of septicemia.

Autopsy eight hours after death. The body is in the same fixed position, especially the lower extremities, that it was *ante mortem*. The bedsore of the posterior surface of the sacrum

space around nucleus and partial
high magnification).



partial chromatolysis and ad-
of nucleus due to destruction of

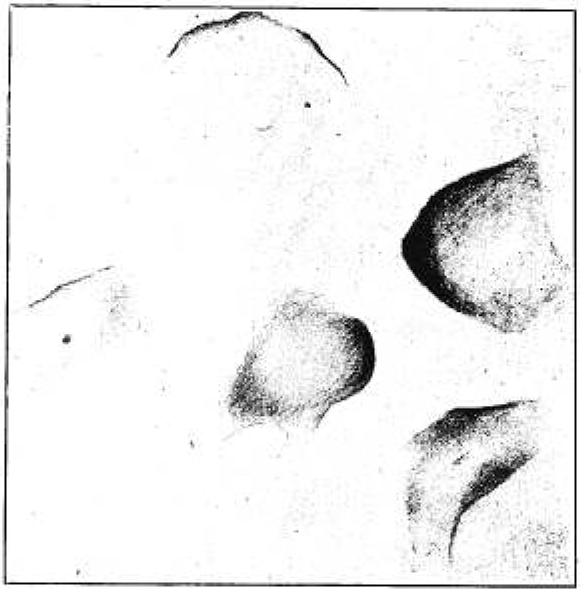


Fig. 4—Swollen homogeneous ventral horn cells. Beginning coagulation of the achromatic substance.

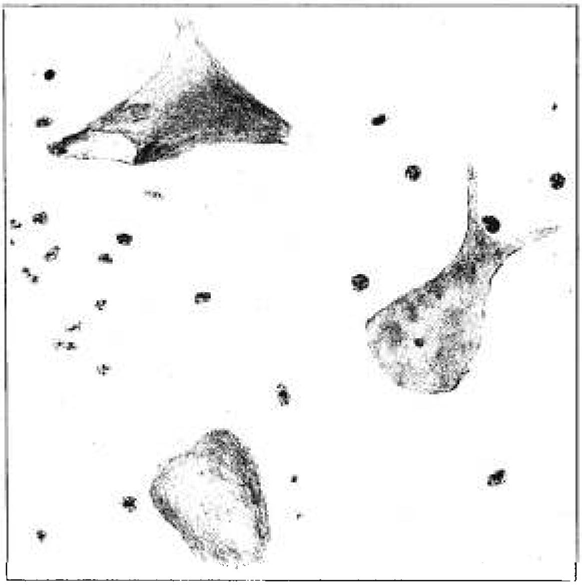


Fig. 5—Fifth lumbar. To show swollen condition of anterior horn cells and homogeneity.

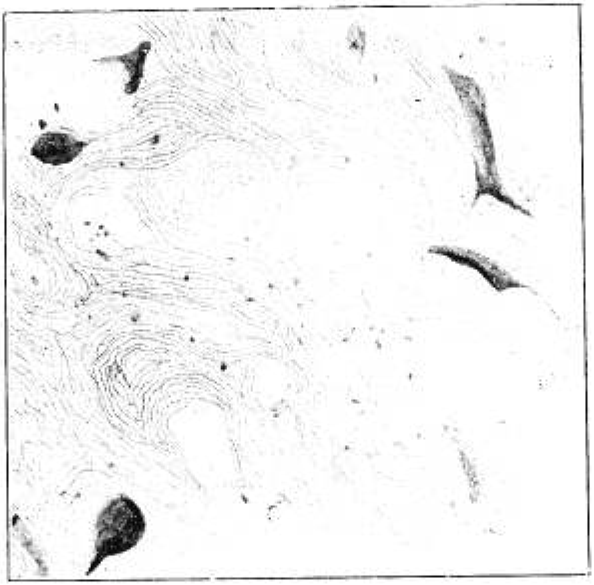


Fig. 2—Second lumbar segment, showing paucity of cells in anterior horns and initiation of degenerative stage in cell substance. Disappearance and dislocation of nuclei.

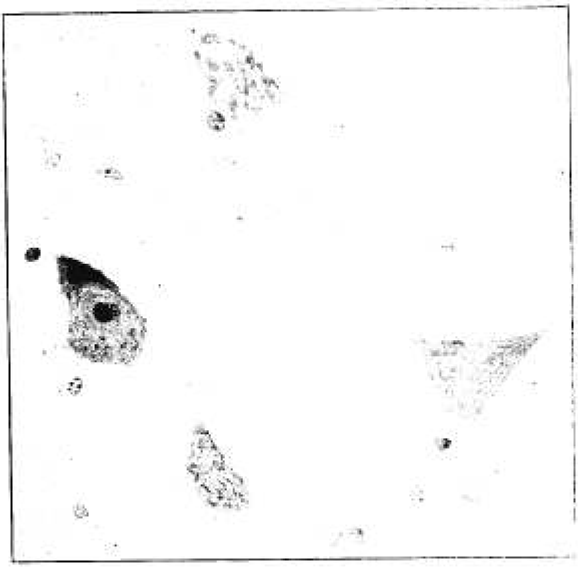


Fig. 3—Second lumbar segment. Anterior horn cells showing varying grades of chromatolysis.

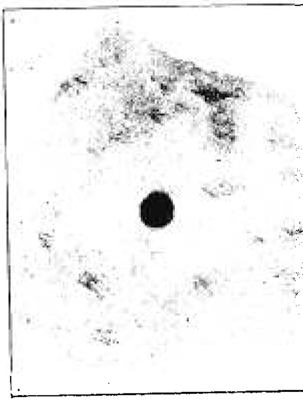
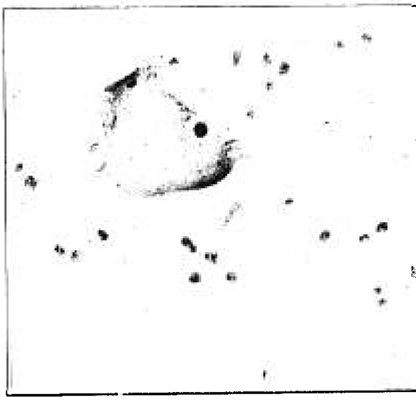


Fig. 6—Enlargement of ce
disappearance of tiger-hide appe



[illegible] d di
[illegible] reticulum.

exposes the bone. On opening the spine, the canal is lined with pus up to the second lumbar vertebra. From this point upward between the pia and dura is a freshly organized layer of greenish yellow exudate, apparently made up of fibrin, pus, and coagulated serum. This layer reaches up through the foramen magnum along the base of the brain and over the optic chiasm. The brain itself is apparently normal. The consistency of the cord is diminished throughout, and from the sixth to the ninth dorsal segments it is so soft that it flows on being cut. The cord was divided into segments and every other one hardened in alcohol and Müller's fluid respectively, preparatory to methylene blue, hematoxylin and carmine stains. Examination of the viscera showed dilatation of the heart, both the right and left sides, and slight fatty degeneration. The lungs were free from tuberculosis. The kidneys were in a state of interstitial and parenchymatous degeneration. No tuberculous foci were found in the thoracic or abdominal viscera.

The changes in the spinal cord on microscopical examination were of variable intensity and distribution. They were most marked in the eighth and ninth dorsal segments, wherein they constituted a focus of central myelitic destruction, surrounded by an annular area of myelomalacia, and were least marked in the cervical cord wherein they consisted of slight perivasculitis, proliferation of neuroglia nuclei, and increased connective tissue formation, both from pial prolongations and from the vessels. The changes in the lumbar segments were most conspicuously evidenced by changes in the substance of the parenchyma. From one end of the cord to the other, the dura was the seat of profound productive inflammation, particularly that portion of it surrounding the posterior segment. The pia was likewise the seat of an exudative and productive inflammation, but it was not implicated so profoundly as the dura.

A number of sections from the different levels of the cord will now be considered in detail, and as the lesion was most intense in the dorsal cord, I shall describe first the changes at this level. The sections made from the eighth dorsal segment and stained according to Weigert and Pal's method show a central area of necrosis, limited in front by the commissure which in some sections is partly, and in others almost wholly destroyed. It is probable that this complete destruction is artificial, as it was very difficult to cut and handle these sections, on account of the destructive changes that had gone on in them during life. Posteriorly, the punched-out area extends about one-third of the distance to the posterior border of the cord. The margin of the focus is made up of detritus and beyond this is an area varying in each section, made up of enlarged and thickened blood vessels, and proliferation of connective tissue with conglomeration of round cells in the perivascular spaces. The pia is very much thickened, especially on the posterior and lateral surfaces of the cord, and sends comparatively few prolongations into the substance. The enormous exudative and proliferative change on the free surface of the pia is very conspicuous in this section. One of the sections from this level stained according to the method of Zeihl, revealed the presence of the bacillus of tuberculosis in the center of a bit of homogeneous material at the margin of the focus of destructive myelitis.

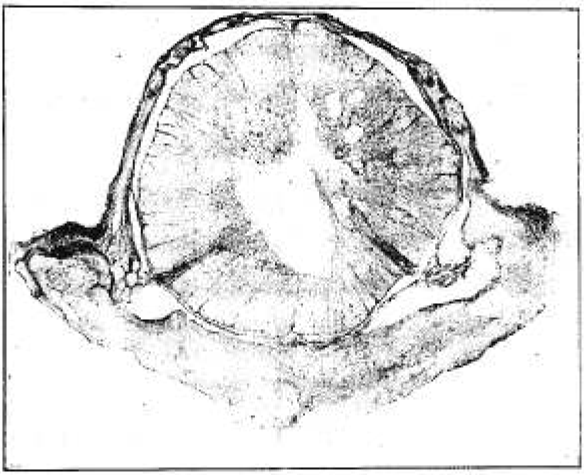


Fig. 1—Eighth dorsal, showing central myelitic focus and a colossal meningeal involvement.

This section was given to the artist to be drawn, but it has been misplaced. The existence of the bacillus was corroborated by Dr. Onuf, by Dr. Harlow Brooks, and others of the staff at the Pathological Institute. No bacilli were found in the meningeal exudate, although many specimens were stained with this end in view. Sections from the lower dorsal levels stained with methylene blue show that the changes in the ganglion cells are those of advanced diffuse chromatolysis. (Here it may be said that the term chromatolysis is used only to mean disintegration of the chromatic particles of the protoplasm.) In some of the cells this chromatolysis is principally peripheral, but in the most it is perinuclear or diffuse. The achromatic part has suffered as well. In many of the cells there is complete disappearance of the achromatic fibrillæ, while in others there is absolute plasmolysis. The cells that were particularly affected at these levels were those of the internal groups of the anterior horns. It is now generally accepted that chromatolysis is the reaction of the cell to a disturbing force and is reparable, while alteration of the achromatic part is degenerative and irreparable. This view is entirely in keeping with the findings in the dorsal segments in which the cell-bodies have lost not only the chromophile but have undergone plasmolysis. The changes of the cells in the upper dorsal and cervical cord are in a measure those that would occur in every spinal cord that had been subject to injurious influences.

Sections from the twelfth dorsal segment, stained according to Weigert, show complete disappearance of the central area of myelitis, but this part of the cord has the appearance of being brittle, and was difficult to section without breaking. Sections from the first lumbar segment stained with Van Gieson's picro-carmine, show thickening of the meninges and the inflammatory exudate. The most noteworthy revelation of this stain, however, was the condition of the blood vessels of the anterior horns; these vessels were seen to be in a state of congestion with resulting transudation and diapedesis, which in part at least conditioned the changes in the ganglion cells of the cord revealed by Nissl's method, which I am about to describe. The degeneration of the white matter of the cord caused by the accompanying meningitis, and revealed by Pal's method, is particularly evident in this and in lower levels of the lumbar cord. Lissauer's column suffered most severely. The central posterior columns were so brittle from the extension of inflammation into them that it was scarcely possible to cut a section without crumbling this part of the cord.

Sections from the various lumbar segments stained with the Nissl stain showed a paucity of cells and a variable degree of degeneration and disintegration of the cell-bodies and processes of the anterior horn. From three to five cell-bodies of each anterior horn were the seat of well-marked degeneration. In some this is so extensive that there is no longer any similarity to normal in the cell-bodies affected, while in others the degeneration is extremely variable. Some of the largest cell-bodies had apparently undergone complete homogeneous transformation, while others show at the periphery narrow marginal lines made up of dots which take a deep blue color, evidently the remains of chromophilic granules. The processes of the cell-bodies show a degeneration very similar to that of the bodies. For instance, some of the processes have the appearance merely of a colorless thread whose continuity, however, can be distinctly traced, but only in one or two places throughout its entire length is there anything like a color dot or spot. Other processes are degenerated at the terminal ends, while the part in connection with the cell-body itself still retains some of the normal longitudinal striation. The cell-bodies which are only partially degenerated preserve to some extent the normal tiger-hide appearance. They have merely undergone some homogeneous transformation which renders them non-receptive to the Nissl stain. The cell-bodies that are least affected show merely an enlargement of the colorless space which normally surrounds the nuclei, and a partial disappearance of the tiger-hide and dotted appearance. The changes in the nuclei of these cell-bodies are variable. In some the nucleus has disappeared, in others it has changed its location from the center of the cell-body, where it is ordinarily found, to the periphery.

The changes in the cell-bodies of the anterior horns of the cervical spinal cord are, especially in the lower segments, very similar to those in the lumbar region, though less pronounced. In the upper cervical cord the structure of the cell-bodies constituting the different groups is not materially altered, despite the fact that the blood vessels of the anterior horns are thickened, the peri-arterial spaces much enlarged, and the neuroglia very much increased. As we proceed downward in our examination of the sections through the cervical cord, we find various manifestations of pathological changes in the cells of the anterior horns. At first there is evidence that the chromophilic granules in many of the cells are large and stained very deeply, while the achromatic substance is quite normal.

Sections from the cervical cord stained with hematoxylin show most strikingly the enormously thickened pia which at these levels is implicated most profoundly over the anterior surface of the cord. This thickened pia extends down the anterior median fissure forcing it widely apart, especially at the bottom, where the pia lies in thick folds extending laterally beneath the columns of Türck, and thence sending prolongations which extend into the anterior horns, the anterior horns themselves being the seat of numerous blood vessels of enlarged caliber and thickened walls. The cell-bodies of the anterior horns from this level when stained with methylene blue show various stages of disintegration in the chromatic substance, with relative preservation of the achromatic substance. In a few sections a blood vessel of the anterior horns cut longitudinally is apparent, and in this diapedesis of the corpuscles can be readily seen. The walls of the blood vessels show very great thickening, especially the internal coat.

As we approach the dorsal region, the cell-bodies of the anterior horns show more marked degenerative changes and are very few in number. A remarkable feature of the cord at this level is the relative preservation of the cell components of Clarke's column. In other sections in which there is conspicuous vascular change in the pial proliferation, the cell-bodies of the anterior horns are relatively well preserved. That the inflammatory process in the meninges of the cervical cord was a relatively recent process, was shown by the fact that although many of the posterior roots at one level or another are completely surrounded and strangulated, as it were, by the thickened meninges, there is despite this very slight ascending degeneration in the posterior columns.

To summarize the clinical history and pathological findings in this case: a young married woman, four months pregnant, is taken ill without attributable cause, with symptoms of acute inflammatory rheumatism. After three weeks, the symptoms subside and are followed by such indications of acute myelitis as motor paralysis of the lower extremities, incontinence of urine, pain in the back and extremities, spasmodic twitchings and contractions of the legs, and enormous bedsores and other associated trophic disturbances. Soon after she gives birth to a living child, the labor being painless. From this time onward the symptoms of meningeal involvement which heretofore had not been conspicuous, become extremely evident. Later, the manifestations of sepsis precede death. On autopsy there is found an extensive purulent and productive leptomeningitis and inflammation of the spinal cord, particularly of the lower dorsal segment. Microscopical examination of this area shows that the focus of most extensive myelitis, consisting of absolute destruction of an area of the central gray matter surrounded by an annular area of myelomalacia, is confined to the seventh, eighth and ninth dorsal segments. The pathological changes in the cellular elements of the cord at these levels are those of extensive, diffuse chromatolysis and plasmolysis, while the changes in the vascular tissues are those of infective inflammation; and those in the white matter of the cord, those of simple inflammation and production of connective tissue. In one section of this level the bacillus of tuberculosis was found imbedded in a mass of caseous necrotic tissue. In the lumbar and cervical segments where there were no evidences of infective inflammation, the cells of the gray matter were found in various stages of chromatolysis, the chromatic substance bearing the brunt of the lesion. Judging from the associated vascular involvement, and the production of neuroglia and connective tissue, the result of marked involvement of the meninges at these levels, these changes in the integral structure of the cell-bodies were the result of these pathological accompaniments as well as of the infectious process which had destroyed the cord at another level.

It seems to me that an interesting point for discussion is the relationship of the rheumatic attack, if rheumatism it really was, to the occurrence of the tuberculous myelitis. Furthermore, it would be interesting to know whether the changes in the cells of remote portions of the cord, constituting chromatolysis, were secondary to the tuberculous infection and the septicemia which immediately conditioned the patient's death, or whether they were the result of nutritional changes due to disease of the blood vessels and impairment of nutrition secondary to the extensive productive inflammation of the meninges.

Personally I am inclined to the view that the patient did not have acute inflammatory rheumatism, but that the pain in the extremities and swelling of the joints which were early symptoms were the result of tuberculous infection of the cord, which implicated in the beginning that part of the cord in which is situated the central representation of the sympathetic nervous system,[1] and that the entire early symptomatology can be explained on this supposition. The symptoms next to develop were the classical ones of slowly progressing acute myelitis, such as the tuberculous variety almost always is. Later, the symptoms of meningitis were superimposed, and they obscured somewhat those due to inflammation of the cord itself.

I reserve further discussion of the pathological features of this case until the publication in this Journal of another article on myelitis.

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[1] See article by Onuf and Collins on this subject in the Archives of Neurology and Psychopathology, Vol. iii, Nos. 1 and 2.